UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,307	12/15/2003	Yu-Fang Hu	P-3641.265	5478

7590 08/25/2006

Jackson Walker L.L.P.
Suite 2100
112 E. Pecan Street
San Antonio, TX 78205

EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 08/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,307	HU ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims **1-12** are pending in this application.

Information Disclosure Statement

The information disclosure statement (IDS filed 2/23/03 has been considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 9, and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3, 9, and 12 respectively contain the trademark/trade name TWEEN (claim 2 and 12) and LIPOSYN, SOYACAL, TRAVEMULSION, INTRALIPID (claim 9). Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a surfactant in claims 3 and 12 respectively and a diluent in claim 9, and accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2, 4-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al (6,350,756) in view of Parikh et al (6,979,456) or vice-versa.

Yang et al teach the use of camptothecin (CPT) analogs including the instantly claimed silatecan, for the treatment of various types of cancer. See abstract and column 28, line 44. Yang et al teach combining the camptothecin analogs with a pharmaceutically acceptable excipient wherein the formulation may be an oral, topical, transdermal, or parenteral in an amount of 1 to 100 mg. See column 10, lines 35-50. Yang teaches the compound for parenteral (IV) administration may be prepared in a form suitable for injection including sterile solutions, dispersions, emulsions, and powders. The diluent may be water, ethanol, glycerols, liquid polyethylene glycol, various oils, and any other known to those skilled in the art. Yang teaches

the final form must be stable under storage conditions. See column 11, lines 40-67. Yang compares the CPT analogs with taxol and notes the increased survival rates. See column 55-56.

Yang does not specify the storage stable injectable composition.

Parikh et al teach an anticancer composition formulated as a self-emulsifying preconcentrate, which is stable. See abstract and column 1, lines 9-15. Parikh teaches various methods have been tried to increase the water solubility of anticancer drugs. See column 1.The preconcentrate comprises an 10-80% of an oil phase, surfactants in an amount of 20-80%, and 0-40% of a hydrophilic component such as propylene glycol and/or ethanol; especially preferred is a combination of ethanol and PPG. See column 5, lines 20-45 and column 3, lines 35-40. The hydrophilic composition must contain at least 6% ethanol. See claim16. Note if the hydrophilic phase comprises at least 6% ethanol, the remaining component is 34% PPG since Parikh teaches the referred combination of ethanol and PPG. The surfactants taught include polyoxyethylene-sorbitan-fatty acid esters and may include a mixture of nonionic surfactants. See column 3 , lines 45-50. The hydrophobic components include triglycerides, propylene glycol dicaprylate/caprate, vegetable oils, etc. See page 6. The preconcentrate may be diluted with water or an appropriate medium before administering. See page 5. The composition is prepared by mixing the oil components, the surfactants, and the drug. See column 7, lines 15-30. For instance, example 5 teaches a preconcentrate comprising 43% Tween 80, soybean oil, 6% ethanol, and 14% Lipoid E80 (phospholipids), among other components.

It would have been obvious to one of ordinary skill in the art at the time the invention was made Yang et al and Parikh et al and utilize Parikh's preconcentrate formulation to formulate Yang's silatecan. One would have been motivated to do so since Parikh teaches a

stable preconcentrate for intravenous administration of water-insoluble anticancer drugs and Yang teaches the compounds may be formulated into any known and conventional composition with the criteria that the formulation is storage stable. Therefore, a skilled artisan would have been motivated to utilize Parikh's vehicle for its improved stability.

Conversely, although Parikh teaches the use of water insoluble anticancer drugs in general, Parikh only exemplifies the anticancer drug taxane. It would have been obvious to one of ordinary skill in the art at the time the invention was made combine the teachings of Parikh et al and Yang et al and utilize the instant anticancer drug, silatecan, in Parikh's stable preconcentrate. One would have been motivated to do so since Parikh teaches a stable preconcentrate that contains a water-insoluble anticancer agent and Yang teaches the CPT analogs including instant silatecan are not only potent, water-insoluble anticancer drugs, the CPT analogs also have a higher survival rate than taxols.

It should be noted that claims 4-9 are not given weight since the claims are directed to intended use of the concentrated emulsion, i.e. wherein the concentrated emulsion formulation is diluted with a diluent *before administration*. The examiner suggests restructuring the claim to remove the intended use phrase. For instance, "the concentrated emulsion further comprising a diluent....".

Claims 1, 3-10, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al (6,350,756) in view of Hamied et al (5,929,030).

Yang et al teach the use of camptothecin (CPT) analogs including the instantly claimed silatecan, for the treatment of various types of cancer. See abstract and column 28, line 44. Yang et al teach combining the camptothecin analogs with a pharmaceutically acceptable excipient

wherein the formulation may be an oral, topical, transdermal, or parenteral in an amount of 1 to 100 mg. See column 10, lines 35-50. Yang teaches the compound for parenteral (IV) administration may be prepared in a form suitable for injection including sterile solutions, dispersions, emulsions, and powders. The diluent my be water, ethanol, glycerols, liquid polyethylene glycol, various oils, and any other known to those skilled in the art. Yang teaches the final form must be stable under storage conditions. See column 11, lines 40-67. Yang compares the CPT analogs with taxol and notes the increased survival rates. See column 55-56.

Yang does not specify the storage stable injectable composition.

Hamied et al teaches a pharmaceutical composition comprising a water-soluble active such as peptides, antimicrobials, and antineoplastics such as taxol. See abstract and column 1, lines 5-14. The stable oil-in-water microemulsion comprises (a) a water insoluble active; (b) hydrophobic phases comprising triglycerides; and (c) phospholipids and other surfactants; and (d) a hydrophilic phase. See column 2, lines 10-30. The preconcentrate comprises 1-12% of the active, 20-80% of an oil phase, 1-10% of a phospholipids, and 10-60% of another surfactant such as polyoxyethylene-sorbitan-fatty acid esters. The hydrophilic phase is generally in an amount of up to 75% and usually 15-50%. See column 3, lines 35-45 and column 4, lines 10-20. The hydrophilic component taught is propylene glycol. See column examples and column 6, lines 1-5. Hamied teaches preparing the composition by mixing lecithin, the other surfactant, the drug, the oil, and propylene glycol.

It would have been obvious to one of ordinary skill in the art at the time the invention was made Yang et al and Hamied et al and utilize Hamied's preconcentrate formulation to formulate Yang's silatecan. One would have been motivated to do so since Hamied teaches a

stable preconcentrate for intravenous administration of water-insoluble anticancer drugs and Yang teaches the compounds may be formulated into any known and conventional composition with the criteria that the formulation is storage stable. Therefore, a skilled artisan would have been motivated to utilize Parikh's vehicle for its improved stability.

Conversely, although Hamied teaches the use of water insoluble anticancer drugs in general, Hamied only exemplifies the anticancer drug taxane. It would have been obvious to one of ordinary skill in the art at the time the invention was made combine the teachings of Hamied et al and Yang et al and utilize the instant anticancer drug, silatecan, in Hamied's stable preconcentrate. One would have been motivated to do so since Hamied teaches a stable preconcentrate that contains a water-insoluble anticancer agent and Yang teaches the CPT analogs including instant silatecan are not only potent, water-insoluble anticancer drugs, the CPT analogs also have a higher survival rate than taxols.

It should be noted that claims 4-9 are not given weight since the claims are directed to intended use of the concentrated emulsion, i.e. wherein the concentrated emulsion formulation is diluted with a diluent *before administration*. The examiner suggests restructuring the claim to remove the intended use phrase. For instance, "the concentrated emulsion further comprising a diluent....".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 4-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of copending Application No. 10/734272 in view of Xiang et al (6,653,319). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

The instant application is directed to an emulsion comprising 4.79-75% of a phospholipids; 24.79-95% PPG, and 0.01-1% of silatecan and a method of preparing the emulsion.

Copending application is directed to a process of producing a liposome suspension comprising mixing an alcohol component, 40-70% phospholipids, 15-30% PEG derived compound, wherein the alcohol to the other components is greater that 5:1 ratio. Dependent claim 2 is directed tot eh alcohol species including PPG, ethanol, methanol, fatty alcohol, glycol, and a combination thereof. Dependent claim 9 is directed to the ratio of alcohol solvent to the other components of 7-10:1. Dependent claim 26 is directed to the drug species including camptothecin. Dependent claims are directed to suspending the liposome in a aqueous medium.

US '272 does not specify the use of silatecan.

Xiang et al teach a camptothecin analogue (silatecan) for treatment of cancer. Xiang teaches silatecan is more lipophilic and intercalates in the liposome better than camptothecin and has higher potency and less toxicity than camptothecin. See column 1, lines 30-40.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine US '272 and Xiang and arrive at the instant invention. One would have been motivated to specifically utilize silatecan instead of camptothecin (CPT) since Xiang teaches silatecan is a CPT analog which has higher potency and less toxicity than camptothecin. Note the instant composition claims are rejected since the process would necessarily yield the instant emulsion. It should be noted that claims 4-9 are not given weight since the claims are directed to intended use of the concentrated emulsion, i.e. wherein the concentrated emulsion formulation is diluted with a diluent *before administration.*

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

All the claims are rejected at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616